Claims 46 and 48 have been amended to be dependent upon claim 52, instead of canceled claim 45.

Claim 46 has also been amended to recite "the expression of said viral genome in said cell is reduced". Support for this amendment is in the specification on page 3, lines 21-23 and page 10, line 5.

New claim 73 has been added to recite the cell of claim 59, wherein the expression of said viral genome or portion thereof in said cell is reduced, wherein said DNA sequences are expressed. Support for this new claim is in the specification on page 6, line 20 and claim 53 as filed.

New claims 74 and 75 have been added to recite the DNA construct of claim 63 and 69 wherein said RNA fragments comprise a nucleotide sequence encode or are derived from a viral coat protein gene, a viral nucleocapsid protein gene, a viral replicase gene, a movement protein gene or portions thereof. Support for this claim is in the specification on page 18, lines 8-10.

Claims 1, 12, 46 and 64 have been amended to recite the methods or DNA construct wherein the expression of the viral genome or portion thereof is reduced. Support for these amendments is in the specification on page 10, lines 1-5.

No new matter has been added by these amendments.

Claim Objections

Claims 45 and 52 have been objected to as being duplicate claims. In response, claim 45 has been canceled without prejudice.

Claims 53-55 and 59-61 have been objected to as being duplicate claims. In response, claims 53-55 have been canceled without prejudice.

These amendments obviate these objections, and Applicants request their withdrawal.

Section 112 Rejection of claims 1-40, 45-70 and 72

Claims 1-40, 45-70 and 72 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for reciting "capable of forming" and "capable of folding".

In order to more particularly point out and distinctly claim subject matter of the present invention, claims 1, 11, 12, 23, 63, 69 and 72 have been amended to recite the RNA molecule "form" or "folds" into a double-stranded RNA molecule or region.

Section 112 Rejection of Claims 46,47, and 53-58

Claims 46, 47 and 53-58 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for reciting "a target gene". In response, in order to more particularly point out and distinctly claim the present invention, claim 46 has been amended to recite "a viral genome

or portion thereof" instead of "a target gene". Claims 53-58 has been canceled without prejudice. Therefore, the above amendments overcome this rejection, and Applicants request its withdrawal.

Section 112 Rejection of Claim 62

Claim 62 is rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for reciting "the two DNA sequences of claim 8". Claim 62 has been amended to recite "the two RNA sequences of claim 8" to correct an obvious typographical error.

Section 112, first paragraph, Rejection of Claims 63-70 and 72

Claims 63-70 and 72 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In particular, the Office Action contends that the claims are broadly directed to any DNA construct expressing sense and antisense RNA fragments of a viral genome or portion thereof, or of any target gene, and allegedly fails to provide a written description of the multitude of isolated DNA molecules encompassed by the claims.

Applicants respectfully disagree with this rejection.

The legal standard for meeting the written description requirement under section 112, first paragraph, is whether "the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar,* 935 F.2d 1555, 1563-64, 19 USPQ2d 1111,1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed.

While Applicants do not agree with this rejection, and in no way acquiesce, claims 66-68 and 72 (directed to a DNA construct with a target gene) has been canceled without prejudice.

The specification as filed meets the requirements for written description of the present invention. The invention encompasses methods of altering or decreasing the expression of a viral genome or portion thereof or a target gene of interest by using a DNA construct comprising a first and second DNA sequence capable of expressing sense and antisense RNA fragments of a viral genome or portion thereof. The viral genome or portion thereof of the present invention are described on page 17, line 27-page 18, line 13. The viruses controlled using the present invention comprise but are not limited to dsDNA viruses, dsRNA viruses, plus-stranded and minus stranded

ssRNA viruses, antisense RNA viruses and retroviruses. Preferred viruses are listed, as are preferred sequences from portions of viruses.

As described above, the specification clearly allows a person of ordinary skill in the art to recognize what has been claimed.

Section 112, first paragraph, Rejection of Claims 1-40, 45-70 and 72

Claims 1-40, 45-70 and 72 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In particular, the Office Action alleges that the instant specification does not demonstrate that the expression of the sense and antisense RNA molecules actually led to alteration of gene expression in cells. The Office Action further states that a declaration presenting data indicating that the expression of the vectors taught in the Examples caused inhibition of gene expression in cells would assist in overcoming this rejection.

Also, the Office Action alleges that "it is unpredictable that such a strategy would be effective to increase viral resistance in non-plant cells." Thus, the Office Action alleges given the breadth of the claims encompassing altering expression of any viral genome in any cell type, unpredictability in the art and alleged lack of guidance of the specification, undue experimentation would be required by one skilled in the art to make and use the claimed invention.

Applicants respectfully disagree with this rejection.

Enablement of a disclosure "is not precluded by the necessity for some experimentation such as routine screening." In re Wands, 858 F.2d 731, 736-7 (Fed. Cir. 1988) (citations omitted). The experimentation necessary must not be undue. Id. At 737. Undue experimentation is experimentation that would require a level of ingenuity beyond what is expected from one of ordinary skill in the field. Fields v. Conover, 170 USPQ 276, 279 (CCPA 1971). The factors that can be considered in determining whether an amount of experimentation is undue have been listed in Wands, 858 F.2d at 737. Among these factors are: the amount of effort involved, the guidance provided by the specification, the presence of working examples, the amount of pertinent literature and the level of skill in the art. The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine. Id.

The relevant inquiry for determining whether the scope of the claims is commensurate with the specification is "whether the scope of enablement provided to one of ordinary skill in the art by the disclosure is such as to be commensurate with the scope of protection sought by the claims." In re

Moore, 439 F.2d 1232, 1236 (CCPA 1971) (emphasis added). "A patent need not teach, and preferably omits, what is well known in the art." Hybridtech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 231 USPQ 81 (Fed. Cir. 1986), cet. Denied, 480 U.S. 947 (1987).

While predictability of the art can be considered in determining whether an amount of experimentation is undue, mere unpredictability of the result of the experiment is not a consideration. Indeed, the Court of Customs and Patent Appeals has specifically cautioned that the unpredictability of the result of an experiment is not a basis to conclude that the amount of experimentation is undue (see In re Angstadt, 190 USPQ 214 (CCPA 1976)).

While Applicants disagree with this rejection, in order to more particularly point out and distinctly claim certain embodiments of the present invention, claims 1, 12, 46 and 64 have been amended to recite the "expression of said viral genome or portion thereof in said cell is reduced." Further, claim 45, 53-55, 66-68 and 72 have been canceled without prejudice.

The specification as filed fully enables the present invention.

Applicants also submit herewith a Declaration of Jan Gielen under 37 C.F.R. § 1.132 (with Exhibits A-C1, C2 and D) providing data demonstrating a decrease in expression of viral genome or portion thereof by following the teaching of the specification, in particular, example 9.

As set forth in the Gielen Declaration, following the description and teachings of the present specification, and using the DNA constructs described therein (in particular in Example 9), one of ordinary skill in the art could practice the invention as claimed. In particular, following the teaching of the specification, one is able to decrease the expression of a viral genome or portion thereof using the DNA constructs described in the specification.

The above remarks, declaration, and amendments overcome and /or obviate the above rejection, and Applicants respectfully request its withdrawal.

Section 112, first paragraph, Rejection of Claims 1-40, 45-70 and 72

Claims 1-40, 45-70 and 72 are rejected under 35 U.S.C. § 112, first paragraph, because while being enabled for inhibiting plant viral protein expression in plant cells, allegedly does not reasonably provide enablement for any other type of alteration of expression of any viral genome. In particular, the claims appear to encompass an alteration in which the expression of viral genome is increased. The Examiner particularly points out that the article by Waterhouse et al., (PNAS, 1998, vol. 95:13960-964) allegedly teaches the same strategy of the instant application induces viral resistance and viral gene silencing in plants and that silencing works via post-transcriptional mechanism. The Examiner suggests the claims be amended to exclude alterations of viral genome expression in which expression is increased.

Applicants respectfully disagree with this rejection. However, in order to more particularly point out and distinctly claim specific embodiments of the present invention, claims 1, 12, 46 and 64 (and claims dependent thereon) have been amended to recite the expression of the viral genome is reduced. Also, claims 45, 53-55, 66-68 and 72 have been canceled without prejudice. These amendments obviate the above rejection, and Applicants request its withdrawal.

Section 102 Rejection of Claims 63, 65 and 66

Claims 63, 65 and 66 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Krueger et al., 1996, Virology 219:301-303. In particular, the Office Action contends that Krueger "teaches" the double-stranded DNA genome of the Feldmannia sp. Virus, and if expressed, sense and antisense RNA fragments would form, and would be capable of forming a double-stranded molecule. "As claim 63, does not require promoters to be present in both DNA strands of the viral genome, Krueger et al. teaches the claimed invention."

Applicants respectfully disagree with this rejection.

The legal test for anticipation under 35 U.S.C. § 102 requires that each and every element of the claimed invention be disclosed or described in a prior art reference in a manner sufficient to enable one skilled in the art to reduce the invention to practice, thus placing the public in possession of the invention. W.L. Gore Assoc. v. Garlock, Inc., 721 F.2d 1540, 1554 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1994); In re Donohue, 766 F.2d 531 (Fed. Cir. 1985). Anticipation under 35 U.S.C. § 102 requires identity of invention. Scripps Clinical & Research Fdn. v. Genentech, Inc., 927 F.2d 1565 (Fed. Cir. 1991).

While the Applicants do not agree with the present rejection, claims 63 (and thus dependent claim 65) has been amended to more particularly point out and distinctly claim the present invention by further reciting the DNA construct comprises a first promoter operably linked to said first DNA sequence and a second promoter operably linked to said second DNA sequence. Also, claim 66 has been cancelled without prejudice.

The above rejection is moot in view of the above amendments, and Applicants request its withdrawal.

The Commissioner is hereby authorized to charge any additional fees under 37 CFR §1.17

which may be required, or credit any overpayment, to Account No. 50-1744 in the name of Syngenta.

A duplicate copy of this letter is provided for charging purposes.

Respectfully submitted,

Timothy Meigs

by Mary Kakefuda

Mary Kakefuda
Agent for Applicants
Reg. No. 39,245

Syngenta Biotechnology Inc.
Patent Department
P.O. Box 12257
Research Triangle Park, NC 27709-2257
(919) 765-5071
Date: July 19, 2001

Version of Specification and Claims with Marked-up Changes

IN THE SPECIFICATION:

Please amend the first paragraph of page 1, as follows:

--This application claims the benefit of U.S. Provisional Application No. [_____] 60/150,705, which was converted on May 10, 1999, from Application No. 09/084,942, filed May 26, 1998 [[] (Heifetz et al., attorney docket no. CGC2010) []] . The disclosure of which is hereby expressly incorporated by reference in its entirety into the instant disclosure.--

IN THE CLAIMS:

Please amend the claims as follows:

1. (amended) A method for conferring resistance or tolerance to a virus upon a cell comprising the step of: introducing into a cell a sense RNA fragment of a viral genome or portion thereof and an antisense RNA fragment of said viral genome or portion thereof, wherein said sense RNA fragment and said antisense RNA fragment [are capable of forming] form a double-stranded RNA molecule, and wherein the expression of said viral genome or portion thereof in said cell is [altered] reduced.

11. (amended) The method of claim 10, wherein said RNA molecule [is capable of folding] folds such that said RNA fragments comprised therein form a double-stranded region.

12. (amended) A method for conferring resistance or tolerance to a virus upon a cell comprising the step of: introducing into a cell a first DNA sequence capable of expressing in said cell a sense RNA fragment of a viral genome or portion thereof and a second DNA sequence capable of expressing in said cell an antisense RNA fragment of said viral genome or portion thereof, wherein said sense RNA fragment and said antisense RNA fragment [are capable of forming] form a double-stranded RNA molecule, and wherein the expression of said viral genome or portion thereof in said cell is [altered] reduced.

23. (amended) The method of claim 22, wherein said RNA molecule [is capable of folding] folds such that said RNA fragments comprised therein form a double-stranded region.

46. (amended) The cell of claim [45] 52, wherein the expression of said [target gene] viral genome or portion thereof in said cell is [altered] reduced by said RNA fragments.

48. (amended) The cell of claim [45] 52, wherein said cell is a plant cell.

62. (amended) A cell comprising the two RNA [DNA] sequences of claim 8, wherein said cell further comprises a sense RNA fragment and an antisense RNA fragment of said [target gene] viral genome or portion thereof.

63. (amended) A DNA construct comprising:
(a) a first DNA sequence capable of expressing in a cell a sense RNA fragment of a viral genome or portion thereof and a second DNA sequence capable of expressing in said cell an antisense RNA fragment of said viral genome or portion thereof, wherein said sense RNA fragment and said antisense RNA fragment [are capable of forming] form a double-stranded RNA molecule,
(b) a first promoter operably linked to said first DNA sequence, and
(c) a second promoter operably linked to said second DNA sequence.

64. (amended) The DNA construct of claim 63, wherein the expression of said viral genome or portion thereof in said cell is [altered] reduced.

69. (amended) A DNA construct comprising a first DNA sequence capable of expressing in a cell a sense RNA fragment of a target gene and a second DNA sequence capable of expressing in said cell an antisense RNA fragment of said target gene, wherein said sense RNA fragment and said antisense RNA fragment [are capable of forming] form a double-stranded RNA molecule, wherein said DNA construct further comprises a bi-directional promoter operably linked to said first DNA sequence and to said second DNA sequence.

Cancel claims 41-44 and 71, without prejudice.
Cancel claims 45 and 53-55, 66-68 and 72 without prejudice.

Please add new claims 73-75 as follows:
--73. (new) The cell of claim 59, wherein the expression of said viral genome or portion thereof in said cell is reduced, wherein said DNA sequences are expressed.

74. (new) The DNA construct of claim 63 wherein said RNA fragments comprise a nucleotide sequence encode or are derived from a viral coat protein gene, a viral nucleocapsid protein gene, a viral replicase gene, a movement protein gene or portions thereof.

75. (new) The DNA construct of claim 69 wherein said RNA fragments comprise a nucleotide sequence encode or are derived from a viral coat protein gene, a viral nucleocapsid protein gene, a viral replicase gene, a movement protein gene or portions thereof.--